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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/614,534	07/07/2003	Zlatko Pflaum	2260/117	9047

2101 7590 05/28/2004

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EXAMINER

SHIAO, REI TSANG

ART UNIT	PAPER NUMBER
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1626

DATE MAILED: 05/28/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 10/614,534	Applicant(s) PFLAUM, ZLATKO	
	Examiner Robert Shiao	Art Unit 1626	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on application filed on 07/07/2003.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-17 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-17 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All b) ☐ Some * c) ☐ None of:
1. ☒ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|---|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date <u>0504</u> . | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

1. This application claims benefit of the foreign application, Slovenia P-9900271 with a filing date 12/10/1999, has not been granted. A English-translated version of the foreign application Slovenia P-9900271 have not been filed. Therefore, the benefit is not being considered until the English translation is perfected.
2. Claims 1-17 are pending in the application.

Claim Rejections - 35 USC § 112

3. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

4. Claims 1-17 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

In claim 1, line 2-5, recites the limitations "solvents of a first type" and "solvents of a second type", are indefinite and ambiguous. Incorporation of the limitation of "solvents of a first type" and "solvents of a second type" into the claims would obviate the rejection, see page 5 lines 15-25 for the first type solvents, and page 6 lines 1-7 for the second type solvents. However, tetrahydrofuran of the first type solvent and hexane of the second type solvent shall not be encompassed, see the below 103(a) rejection.

Claim Rejections - 35 USC § 103

5. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 1-17 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kumar et al. US 6,528,660. Kumar et al. "660 is a 102(e) reference.

Applicants claim a process of preparing atorvastatin in an amorphous form, which comprises:

a) providing a solution of atorvastatin in one or more solvents of a first type such that atorvastatin is freely soluble; b) providing a mixture of said atorvastatin solution with one or more solvents of a second type, in which atorvastatin is insoluble or very slightly soluble, such that atorvastatin precipitates; and c) separating the precipitate formed in step (b) from the mixture of solvents.

The instant processes are found in the pages 1-9 of the specification.

Determination of the scope and content of the prior art (MPEP §2141.01)

Kumar et al. disclose process methods for preparing amorphous atorvastatin calcium. The process methods are the following steps:

(a) dissolving crystalline atorvastatin calcium in a non-hydroxylic solvent, see column 2 lines 11-67 The non-hydroxylic solvent is tetrahydrofuran or other solvents, see

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column 2, lines 47-65; (b) adding a non-polar hydrocarbon anti-solvent to precipitate out atorvastatin calcium, see column 2, line 44-45. The non-polar hydrocarbon solvent is n-hexane, or hexane fraction, or other solvents, see column 2, lines 50-55; and (c) removing the solvent by filtration to afford amorphous atorvastatin calcium, see column 2, 9 lines 46-47.

Determination of the difference between the prior art and the claims (MPEP

§2141.02)

Kumar et al. disclose that crystalline atorvastatin calcium is the starting material for preparing amorphous atorvastatin calcium. However, in the instant application, solid atorvastatin is used for the starting material. The solid atorvastatin is crystalline atorvastatin, or mixture of crystalline and/or polycrystalline and amorphous atorvastatin, see page 3 lines 19 –27. It is noted that crystalline atorvastatin calcium is innate nature of solid atorvastatin.

Kumar et al. disclose that crystalline atorvastatin calcium is dissolved in the non-hydroxylic solvent tetrahydrofuran, see column 2, lines 47-65. In the instant application, however, atorvastatin is dissolved in the first type solvent including tetrahydrofuran and other solvents, see instant claim 1 step (a) and page 5 lines 15-25 of the specification.

Kumar et al. disclose that atorvastatin calcium can be precipitated out by adding non-polar hydrocarbon anti-solvent, which is n-hexane, or hexane fraction, or other solvents, see column 2 lines 44-45. In the instant application, however, the second type

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solvent is hexane, or diethyl ether, or other solvents, is added to precipitate out atorvastatin, see claim1 step (b) and page 4 lines 5-19 of the specification.

Both Kumar et al. and instant application disclose that filtration is the subsequent method to separate amorphous atorvastatin from solvent, see column 3 line 16-22 of Kumar et al. and step (c) of the instant claim 1 and page 4 lines 20-24 of the instant specification.

Finding of prima facie obviousness-rational and motivation (MPEP §2142-2143)

One having ordinary skill in the art would find the claims prima facie obvious **because** processes for preparing amorphous atorvastatin has been disclosed by Kumar et al. The employment of an obvious modification of Kumar et al. processes of preparing amorphous atorvastatin, using starting material solid atorvastatin or crystalline atorvastatin calcium, first type solvent tetrahydrofuran, second type solvent n-hexane, and subsequent filtration method to separate the precipitate from solvent to obtain amorphous atorvastatin, is considered prima facie obvious in the absence of unexpected results.

Double Patenting

6. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11

F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

7. Claims 1-17 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claim 1 of Pflaum's 6,613,916. Although the conflicting claims are not identical, they are not patentably distinct from each other and reasons are as follows.

Applicants claim a process of preparing atorvastatin in an amorphous form, which comprises:

a) providing a solution of atorvastatin in one or more solvents of a first type such that atorvastatin is freely soluble; b) providing a mixture of said atorvastatin solution with one or more solvents of a second type, in which atorvastatin is insoluble or very slightly

soluble, such that atorvastatin precipitates; and c) separating the precipitate formed in step (b) from the mixture of solvents.

The instant processes are found in the pages 1-9 of the specification.

Pflaum claims a process for the preparation of atorvastatin in an amorphous form, which comprises: a) providing a solution of atorvastatin in one or more solvents of a first type such that atorvastatin is freely soluble; b) providing a mixture of said atorvastatin solution with one or more solvents of a second type, in which atorvastatin is insoluble or very slightly soluble, such that atorvastatin precipitates; and c) separating the precipitate formed in step (b) from the mixture of solvents; wherein the solvent of the first type is selected from low molecular alcohols, ketones and esters, and the solvent of the second type is an ether solvent.

The difference between the instant claims and Pflaum's is that the instant claims silence the specific solvent of the first and second type solvent.

One having ordinary skill in the art would find the instant claims *prima facie* obvious **because** one would be motivated to employ the processes of Pflaum's to obtain a process of preparing atorvastatin in an amorphous form, wherein the first (i.e., low molecular alcohols) or second type solvent (ether solvent) are used.

The motivation to make the claimed compounds derives from the expectation that the instant claimed processes would obtain similar yields from the known Pflaum's processes to that which is claimed in the reference.


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Telephone Inquiry

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Robert Shiao whose telephone number is (571) 272-0707. The examiner can normally be reached on 8:30 AM - 5:00 PM.

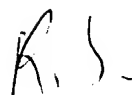
If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Joseph K. McKane can be reached on (571) 272-0699. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).



Joseph K. McKane
Supervisory Patent Examiner
Art Unit 1626

5/26/04



Robert Shiao, Ph.D.
Patent Examiner
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May 26, 2004